253.182

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	:	E. Prats
M. SIEIJN et al	:	
Serial No.: 402,604	:	Group: 1651
Filed: October 22, 1999	:	
For: ISOLATION...BIOMASS	:	

600 Third Avenue
New York N.Y. 10016
November 12, 2001

RULE 116 AMENDMENT

Asst. Commissioner for Patents
Washington, D.C. 20231

Sir:

Responsive to the office action of June 20, 2001, please amend this application as follows:

Claim 1 (twice amended) A process for the isolation of crystalline carotenoid compound from microbial biomass comprising disrupting the microbial cell walls, separating cellular debris from the resulting carotenoid crystal containing residue, washing carotenoid crystal containing residue with a solvent to remove lipid, suspending the obtained carotenoid crystals in water to float the crystals and remove biomass debris, recovering the crystals and, optionally, further purifying the crystals.

REMARKS

Reconsideration of this application is requested in view of the proposed amendments to the claims and the remarks presented herein. Entry of the amendment is requested under the provisions of Rule 116 as it puts the application in better condition for

appeal.

The claims in the application are claims 1 to 14, no other claims having been presented.

Applicants' attorney wishes to thank the Examiner in charge of the application for the courtesies extended to him at the interview on November 8, 2001 at which time, the final rejection was discussed.

Claim 1 has been amended to correct the term "residue" and has been further amended to more clearly point out that the crystals reside in the residue throughout the process. Therefore, entry of the amendment is believed proper under the provisions of Rule 116.

All of the claims stand rejected under 35 USC 103 as being obvious over the Jaeger et al patent taken in view of the Sarnecki patent and optionally with the Rose et al patent for reasons of record.

Applicants respectfully traverse this ground of rejection since the Jaeger et al patent is an example of the prior art that Applicants wish to avoid. The main feature of Applicants' invention is the direct isolation of ß-carotene type material from a microbial biomass wherein the direct isolation is effected by obtaining the ß-carotene crystals from a fermentation process

without any solvent extraction. Applicants' process uses a washing step to remove lipids from the biomass and then the resulting carotenoid crystals are suspended in water to float the crystals thereon and to remove the biomass debris after which, the crystals are recovered.

In contrast thereto, Jaeger et al describes a process wherein the ß-carotene producing cells are extracted with a solvent followed by crystallization of ß-carotene. As pointed out to the Examiner at the interview, there is a distinct difference between washing and extracting. During a washing step, a solid material is treated with a solvent to remove impurities from the surface of the solid and extraction is a treatment of a solid product with an extraction solvent to dissolve the compound therein after which, there is a crystallization effected by various techniques such as solvent evaporation or cooling but as can be seen from pages 1 and 2 of the application as filed, the use of solvent extraction is what Applicants wish to avoid. In contrast thereto, Applicants merely wash the crystals to remove any lipid on the crystals thereof while leaving the ß-carotene in crystalline form. The resulting washed crystals are then suspended in water to float the crystals thereon and to remove biomass debris after which, the crystals are recovered. There is absolutely no extraction step whatsoever in Applicants' process and the Jaeger et al patent cited by the Examiner is what Applicants' wish to avoid. Therefore, withdrawal of this ground of rejection is requested.

In view of the proposed amendments to the claims and the above remarks, it is believed that the claims clearly point out Applicants' patentable contribution and favorable reconsideration of the application is requested.

Respectfully submitted,
Bierman, Muserlian and Lucas

By: _____
Charles A. Muserlian #19,683
Attorney for Applicants
Tel.# (212) 661-8000

CAM:ds
Encl.: Marked up copy of claim 1

CERTIFICATION OF FACSIMILE TRANSMISSION

I hereby certify that this paper is being facsimile transmitted to the Patent and Trademark Office on the date shown below.

Charles A. Muserlian

_____ November 12, 2001

MARKED UP VERSION OF CLAIM
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600 Third Avenue
New York N.Y. 10016
April 24, 2001

AMENDMENT

Asst. Commissioner for Patents
Washington, D.C. 20231

Sir:

Responsive to the office action of February 2, 2001, please amend this application as follows:

IN THE SPECIFICATION:

Please add as the last page of the application the Abstract of the Disclosure submitted herewith on a separate sheet of paper.

IN THE CLAIMS:

Claim 1 (amended) A process for the isolation of crystalline carotenoid compound from microbial biomass comprising disrupting the microbial cell walls, separating cellular debris from the carotenoid-containing residue, washing one member of the group consisting of the microbial biomass, the disrupted cell mass and the carotenoid-containing reside with a solvent to remove lipid, suspending the obtained carotenoid crystals in water to float the crystals, and Remove biomass debris recovering the crystals and, optionally, further purifying the crystals.

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Sir:

Responsive to the office action of February 2, 2001, please amend this application as follows:

IN THE SPECIFICATION:

Please add as the last page of the application the Abstract of the Disclosure submitted herewith on a separate sheet of paper.

IN THE CLAIMS:

Claim 1 (amended) A process for the isolation of crystalline carotenoid compound from microbial biomass comprising disrupting the microbial cell walls, separating cellular debris from the carotenoid-containing residue, washing one member of the group consisting of the microbial biomass, the disrupted cell mass and the carotenoid-containing reside with a solvent to remove lipid, suspending the obtained carotenoid crystals in water to float the crystals, and remove biomass debris recovering the crystals and, optionally, further purifying the crystals.

Claim 2 (amended) The process of claim 1, wherein the carotenoid-containing residue is washed with a solvent to remove lipid.

Claim (4 (twice amended) The process of claim 1, wherein the solvent to remove lipid is a lower alcohol or acetone.

Claim 5 (twice amended) The process of claim 1, wherein a solvent immiscible with water is added to the microbial cells before, during or after disrupting the cell walls.

Claim 6 (amended) The process of claim 5, wherein said solvent immiscible with water is added to the disrupted cell mass after disrupting the cell walls.

Claim 7 (twice amended) The process of claim 5, wherein said solvent immiscible with water is an oil.

Claim 8 (twice amended) The process of claim 1, wherein floating of the crystals is effected with bubbling of a gas through the suspension.

Add the following claims:

--13. The process of claim 4 wherein the solvent is ethanol.

14. The process of claim 7 wherein the oil is a vegetable oil.--

REMARKS

Reconsideration of this application is requested in view of the amendments to the specification and claims and the remarks presented herein.

The claims in the application are claims 1 to 14, no other claims having been presented.

Applicants are submitting herewith an Abstract of the Disclosure on a separate sheet of paper.

All of the claims were rejected under 35 USC 112, second paragraph, as being indefinite. The Examiner objected to the "preferable" clause and to the term "suitable".

Applicants respectfully traverse these grounds of rejection since the amended claims are believed to properly define the invention. The preferred clauses have been removed from claims 4 and 7 and they have presented as new claims 13 and 14. The claims have been amended to conform to the American practice and therefore, are believed to comply with 35 USC 112. Therefore, withdrawal of this ground of rejection is requested.

Claims 1 to 9, 11 and 12 were rejected as being obvious over the Jaeger patent taken in view of the Sarnecki patent. All of the claims were rejected as being obvious over the Jaeger patent taken in view of the Sarnecki patent and further, in view of the Rose et al and Bohinski patents. The Examiner states that Jaeger discloses obtaining ß-carotene from a biomass which is treated with a solvent and extracted with a water immiscible solvent and the ß-carotene is then crystallized from an organic solvent. Sarnecki is cited to

show solvent extracted ß-carotene being readily crystallized in water in a highly pure form. The tertiary references are cited to show the use of a vegetable oil at various times of the extraction process. The Examiner deems that the claimed process would be obvious therefrom.

Applicants respectfully traverse these grounds of rejection since the amended claims are clearly distinct and not anticipated by the prior art cited by the Examiner. The main feature of Applicants' invention is the direct isolation of ß-carotene type material from a microbial mass which direct isolation is effected by obtaining ß-carotene crystals from a fermentation process without any solvent extraction. Applicants' process uses a washing step to remove lipids from the biomass and then an aqueous floatation step to separate the crystals from the biomass debris. There is no dissolution of the ß-carotene crystals as is necessary in a solvent extraction process.

In contrast thereto, Jaeger describes a process wherein the ß-carotene producing cells are extracted with a solvent followed by crystallization of ß-carotene. The Rose et al reference shows a solvent extraction process in which the organic solvent is a vegetable oil followed by membrane separation of the organic and aqueous phases. The Bohinski patent describes a fermentation process and advocates the use of vegetable oils during the fermentation to enhance the yield of the fermentation process. The

Bohinski patent makes no mention of any procedure for recovering the ß-carotene obtained during fermentation.

The Sarnecki patent describes a process for purifying ß-carotene by treating crude ß-carotene crystals with a surfactant followed by washing with water and not water alone. There is no mention made of a fermentation broth as a starting material for the purification process. The prior art cited by the Examiner relates to a solvent extraction process which the present process is intended to avoid. Therefore, withdrawal of this ground of rejection is requested.

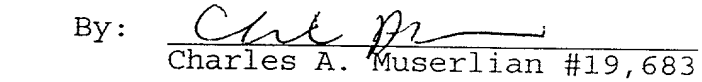
All of the claims were rejected under obviousness type double patenting with respect to the claims of copending application Serial No. 09/214,375 because allegedly, both processes have the same basic process steps, namely, disruption of cells containing ß-carotene, solvent extraction with an organic solvent and crystallization in water.

Applicants respectfully traverse this ground of rejection since the copending application is in no way directed to the present process. For the Examiner's convenience, Applicants are submitting herewith a copy of claims 18 to 28 as they appear in the copending application. The said copending application is directed to a means of obtaining highly purified ß-carotene crystals from a natural source using a solvent extraction procedure for the

isolation of ß-carotene. As noted above, Applicants' process is intended to avoid solvent extraction and uses a washing step to remove lipids and then an aqueous floatation step to obtain the ß-carotene. The two processes are entirely different and the double patenting rejection is improper.

In view of the amendments to the specification and claims and the above remarks, it is believed that the claims clearly point out Applicants' patentable contribution and favorable reconsideration of the application is requested.

Respectfully submitted,
Bierman, Muserlian and Lucas

By: 
Charles A. Muserlian #19,683
Attorney for Applicants
Tel.# (212) 661-8000

CAM:ds
Enclosures

Claims

1. A process for the isolation of a crystalline carotenoid compound from microbial biomass comprising ~~the steps of~~ disrupting the microbial cell walls, separating cellular debris from the carotenoid-containing residue, ~~including a~~ washing of ~~either~~ the microbial biomass, the disrupted cell mass ~~or~~ the carotenoid-containing residue with a solvent ~~suitable~~ to remove lipid, suspending the obtained carotenoid crystals in water to float the crystals, recovering the crystals and, optionally, further purifying the crystals.

2. The process of claim 1, wherein the carotenoid-containing residue is washed with a solvent ~~suitable~~ to remove lipid.

3. The process of claim 2, wherein the carotenoid-containing residue is washed with water prior to lipid removal.

4. The process of any one of the claims 1 to 3, wherein the solvent ~~suitable~~ to remove lipid is a lower alcohol or acetone, ~~preferably~~ ethanol.

5. The process of any one of the claims 1 to 4, wherein a solvent ~~not~~ immiscible with water is added to the microbial cells before, during or after disrupting the cell walls.

6. The process of claim 5, wherein said solvent ~~not~~/miscible with water is added to the disrupted cell mass after disrupting the cell walls.

7. The process of claim 5 or 6, wherein said solvent ~~not~~/miscible with water is an oil, ~~preferably a vegetable oil~~.

8. The process of any one of the claims 1 to 7, wherein floating of the crystals is ~~improved by~~ bubbling/gas through the suspension.